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(FILE 'HOME' ENTERED AT 14:08:48 ON 23 SEP 2002)

INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,  
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO,  
CABA,  
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,  
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 14:08:59 ON  
23 SEP 2002

SEA FUCOSYLATION

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L1

QUE FUCOSYLATION

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FILE 'CAPLUS, EMBASE, BIOSIS, SCISEARCH, MEDLINE, BIOTECHNO, ESBIODASE,  
CANCERLIT' ENTERED AT 14:10:01 ON 23 SEP 2002

L2 57 S L1 (S) (FUCT-IV OR FUCT-VI OR FUCT-VII)  
L3 21 S L2 (S) (GLYCOPEPTIDE OR ACCEPTOR)  
L4 9 S L3 (S) (VITRO)  
L5 4 DUP REM L3 (17 DUPLICATES REMOVED)  
L6 2 DUP REM L4 (7 DUPLICATES REMOVED)

=> d 15 ibib ab 1-4

L5 ANSWER 1 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1  
ACCESSION NUMBER: 2000292023 EMBASE  
TITLE: Localization of .alpha.1,3-fucosyltransferase VI in  
Weibel-Palade bodies of human endothelial cells.  
AUTHOR: Schnyder-Candrian S.; Borsig L.; Moser R.; Berger E.G.  
CORPORATE SOURCE: E.G. Berger, Institute of Physiology, University of  
Zurich,  
Winterthurerstrasse 190, CH-8057 Zurich, Switzerland.  
egberger@physiol.unizh.ch  
SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America, (18 Jul 2000) 97/15 (8369-8374).  
ISSN: 0027-8424 CODEN: PNASA6  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Surface glycosylation of endothelial cells is relevant to various  
processes including coagulation, inflammation, metastasis, and lymphocyte  
homing. One of the essential sugars involved in these processes is fucose  
linked .alpha.1,3-fucose to N-acetylglucosamine. A family of  
.alpha.1,3-fucosyltransferases (FucTs) called FucT-III, IV, V, VI, VII,  
and IX is able to catalyze such **fucosylations**. Reverse  
transcription-PCR analysis revealed that human umbilical vein endothelial  
cells express all of the FucTs except FucT-IX. The predominant activity,  
as inferred by **acceptor** specificity of enzyme activity in cell  
lysates, is compatible with the presence of **FucT-VI**.  
By using an antibody to recombinant soluble **FucT-VI**,  
the enzyme colocalized with .beta.4-galactosyltransferase-1 to the Golgi  
apparatus. By using a polyclonal antiserum raised against a 17-aa peptide  
of the variable (stem) region of the **FucT-VI**,  
immunocytochemical staining of **FucT-VI** was restricted  
to Weibel-Palade bodies, as determined by colocalization with P-selectin  
and von Willebrand factor. SDS/PAGE immunoblotting and amino acid  
sequencing of internal peptides confirmed the identity of the antigen  
isolated by the peptide-specific antibody as **FucT-VI**.  
Storage of a fucosyltransferase in Weibel-Palade bodies suggests a  
function independent of Golgi-associated glycosylation.

L5 ANSWER 2 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2  
ACCESSION NUMBER: 1999041397 EMBASE  
TITLE: ~~In vitro .alpha.1-3 or .alpha.1-4 fucosylation of type I~~  
~~and II oligosaccharides with secreted forms of recombinant~~  
~~human fucosyltransferases III and VI.~~  
AUTHOR: Nimtz M.; Grabenhorst E.; Gamber U.; Costa J.; Wray V.;  
Morr M.; Thiem J.; Conradt H.S.  
CORPORATE SOURCE: M. Nimtz, Gesellschaft Biotechnol. Forschung, Mascheroder  
Weg 1, 38124 Braunschweig, Germany  
SOURCE: Glycoconjugate Journal, (1998) 15/9 (873-883).  
Refs: 25  
ISSN: 0282-0080 CODEN: GLJOEW  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
029 Clinical Biochemistry  
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Transgalactosylation of chitobiose and chitotriose employing .beta.-galactosidase from bovine testes yielded mixtures with .beta.1-3 linked galactose (type I) and .beta.1-4 linked galactose (type II) in a final ratio of 1:1 for the tri- and 1:1.4 for the tetrasaccharide. After 24 h incubations of the two purified oligosaccharide mixtures with large amounts (20-fold increase compared with standard conditions) of human .alpha.1, 3/4-fucosyltransferase III (FucT III), the type I tri-/tetrasaccharides were completely converted to the Lewis structure, whereas approximately 10% **fucosylation** of the type II isomers to the Lewis(x) oligosaccharides was observed in long-term incubations. Employing large amounts of human .alpha.1, 3-fucosyltransferase VI (FucT VI), the type I trisaccharide substrate was exclusively fucosylated at the proximal 0-4 substituted N-acetylglucosamine (GlcNAc) (20%) whereas almost all of the type II isomers was converted to the corresponding Lewis(x) product. 45% of the type I tetrasaccharide was fucosylated at the second GlcNAc solely by FucT VI. The type II isomer was almost completely .alpha.1-3 fucosylated to yield the Lewis(x) derivative with traces of a structure that contained an additional fucose at the reducing GlcNAc. The results obtained in the present study employing high amounts of enzyme confirmed our previous results that FucT III acts preponderantly as a .alpha.1-4 fucosyltransferase onto GlcNAc in vitro. Human FucT VI attaches fucose exclusively in an .alpha.1-3 linkage to 4-substituted GlcNAc in vitro and does not modify any 3-substituted

GlcNAc to yield Lewis oligosaccharides. With 8-methoxycarbonyloctyl glycoside **acceptors** used under standard conditions, FucT III acts exclusively on the type I and FucT VI only on the type II derivative. With lacto-N-tetraose, lacto-N-fucopentaose I, or LS-tetrasaccharide as substrates, FucT III modified the 3-substituted GlcNAc and the reducing glucose; FucT VI recognized only lacto-N-neotetraose as a substrate.

L5 ANSWER 3 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3  
ACCESSION NUMBER: 1998136828 EMBASE  
TITLE: Acceptor specificity of the human leukocyte .alpha.3 fucosyltransferase: Role of FucT-VII in the generation of selectin ligands.  
AUTHOR: Britten C.J.; van den Eijnden D.H.; McDowell W.; Kelly V.A.; Witham S.J.; Edbrooke M.R.; Bird M.I.; de Vries T.; Smithers N.  
CORPORATE SOURCE: C.J. Britten, Glycobiology Research Unit, GlaxoWellcome Res. and Devt. Ltd., Medicines Research Centre, Stevenage, Herts, SG1 2NY, United Kingdom  
SOURCE: Glycobiology, (1998) 8/4 (321-327).  
Refs: 35  
ISSN: 0959-6658 CODEN: GLYCE3  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The .alpha.3 fucosyltransferase, **FucT-VII**, is one of the key glycosyltransferases involved in the biosynthesis of the sialyl Lewis X (sLe(x)) antigen on human leukocytes. The sialyl Lewis X antigen (NeuAc.alpha.(2-3)Gal.beta.(1-4)[Fuc.alpha.(1-3)]GlcNAc-R) is an essential component of the recruitment of leukocytes to sites of inflammation, mediating the primary interaction between circulating leukocytes and activated endothelium. In order to characterize the enzymatic properties of the leukocyte .alpha.3 fucosyltransferase **FucT-VII**, the enzyme has been expressed in *Trichoplusia ni* insect cells. The enzyme is capable of synthesizing both sLe(x) and sialyl-dimeric-Le(x) structures in vitro, from 3'-sialyl-lacNAc and

VIM-2

structures, respectively, with only low levels of fucose transfer observed to neutral or 3'-sulfated **acceptors**. Studies using fucosylated NeuAc.alpha.(2-3)- (Gal.beta.(1-4)GlcNAc)3-Me **acceptors** demonstrate that **FucT-VII** is able to synthesize both di-fucosylated and trifucosylated structures from mono- fucosylated precursors, but preferentially fucosylates the distal GlcNAc within a polylactosamine chain. Furthermore, the rate of **fucosylation** of the internal GlcNAc residues is reduced once fucose has been added to the distal GlcNAc. These results indicate that **FucT-VII** is capable of generating complex selectin ligands, in vitro, however the order of fucose addition to the lactosamine chain affects the rate of selectin ligand synthesis.

L5 ANSWER 4 OF 4 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4

ACCESSION NUMBER: 95120994 EMBASE

DOCUMENT NUMBER: 1995120994

TITLE: Acceptor specificity of different length constructs of human recombinant .alpha.1,3/4-fucosyltransferases. Replacement of the stem region and the transmembrane

domain

of fucosyltransferase V by protein A results in an enzyme with GDP-fucose hydrolyzing activity.

AUTHOR: De Vries T.; Srnka C.A.; Palcic M.M.; Swiedler S.J.; Van den Eijnden D.H.; Macher B.A.

CORPORATE SOURCE: Dept. of Medical Chemistry, Vrije Universiteit, Van der Boechorststraat 7, 1081 BT Amsterdam, Netherlands

SOURCE: Journal of Biological Chemistry, (1995) 270/15 (8712-8722).

ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The **acceptor** specificity of recombinant full-length, membrane-bound fucosyltransferases, expressed in COS-7 cells, and soluble,

protein-A chimeric forms of .alpha.1,3-fucosyltransferase (Fuc-T) III, Fuc-TIV, and Fuc-TV was analyzed toward a broad panel of oligosaccharide, glycolipid, and glycoprotein substrates. Our results on the full-length enzymes confirm and extend previous studies. However, chimeric Fuc-Ts showed increased activity toward glycoproteins, whereas chimeric Fuc-TIII and Fuc-TV had a decreased activity with glycosphingolipids, compared to the full-length enzymes. Unexpectedly, chimeric Fuc-TV exhibited a GDP-fucose hydrolyzing activity. In substrates with multiple **acceptor** sites, the preferred site of **fucosylation** was identified. Fuc-TIII and Fuc-TV catalyzed fucose transfer exclusively to OH-3 of glucose in lacto-N-neotetraose and lacto-N-tetraose, respectively,

as was demonstrated by 1H NMR spectroscopy. Thin layer chromatography immunostaining revealed that **FucT-IV** preferred the distal GlcNAc residue in nLc6Cer, whereas Fuc-TV preferred the proximal GlcNAc residue. Incubation of Fuc-TIV or Fuc-TV with VI3NeuAcnLc6Cer resulted in products with the sialyl-Lewis(X) epitope as well as the

VIM-2

structure. To identify polar groups on **acceptors** that function in enzyme binding, deoxygenated substrate analogs were tested as **acceptors**. All three Fuc-Ts had an absolute requirement for a hydroxyl at C-6 of galactose in addition to the accepting hydroxyl at C-3 or C-4 of GlcNAc.

L6 ANSWER 1 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1  
ACCESSION NUMBER: 1999041397 EMBASE  
TITLE: In vitro .alpha.1-3 or .alpha.1-4 fucosylation of type I and II oligosaccharides with secreted forms of recombinant human fucosyltransferases III and VI.  
AUTHOR: Nimtz M.; Grabenhorst E.; Gamber U.; Costa J.; Wray V.; Morr M.; Thiem J.; Conradt H.S.  
CORPORATE SOURCE: M. Nimtz, Gesellschaft Biotechnol. Forschung, Mascheroder Weg 1, 38124 Braunschweig, Germany  
SOURCE: Glycoconjugate Journal, (1998) 15/9 (873-883).  
Refs: 25  
ISSN: 0282-0080 CODEN: GLJOEW  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Transgalactosylation of chitobiose and chitotriose employing .beta.-galactosidase from bovine testes yielded mixtures with .beta.1-3 linked galactose (type I) and .beta.1-4 linked galactose (type II) in a final ratio of 1:1 for the tri- and 1:1.4 for the tetrasaccharide. After 24 h incubations of the two purified oligosaccharide mixtures with large amounts (20-fold increase compared with standard conditions) of human .alpha.1, 3/4-fucosyltransferase III (FucT III), the type I tri-/tetrasaccharides were completely converted to the Lewis structure, whereas approximately 10% **fucosylation** of the type II isomers to the Lewis(x) oligosaccharides was observed in long-term incubations. Employing large amounts of human .alpha.1, 3-fucosyltransferase VI (**FucT VI**), the type I trisaccharide substrate was exclusively fucosylated at the proximal 0-4 substituted N-acetylglucosamine (GlcNAc) (20%) whereas almost all of the type II isomers was converted to the corresponding Lewis(x) product. 45% of the type I tetrasaccharide was fucosylated at the second GlcNAc solely by **FucT VI**. The type II isomer was almost completely .alpha.1-3 fucosylated to yield the Lewis(x) derivative with traces of a structure that contained an additional fucose at the reducing GlcNAc. The results obtained in the present study employing high amounts of enzyme confirmed our previous results that FucT III acts preponderantly as a .alpha.1-4-fucosyltransferase onto GlcNAc in **vitro**. Human **FucT VI** attaches fucose exclusively in an .alpha.1-3 linkage to 4-substituted GlcNAc in **vitro** and does not modify any 3-substituted GlcNAc to yield Lewis oligosaccharides. With 8-methoxycarbonyloctyl glycoside **acceptors** used under standard conditions, FucT III acts exclusively on the type I and **FucT VI** only on the type II derivative. With lacto-N-tetraose, lacto-N-fucopentaose I, or LS-tetrasaccharide as substrates, FucT III modified the 3-substituted GlcNAc and the reducing glucose; **FucT VI** recognized only lacto-N-neotetraose as a substrate.

L6 ANSWER 2 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2  
ACCESSION NUMBER: 1998136828 EMBASE  
TITLE: Acceptor specificity of the human leukocyte .alpha.3 fucosyltransferase: Role of FucT-VII in the generation of selectin ligands.  
AUTHOR: Britten C.J.; van den Eijnden D.H.; McDowell W.; Kelly V.A.; Witham S.J.; Edbrooke M.R.; Bird M.I.; de Vries T.; Smithers N.  
CORPORATE SOURCE: C.J. Britten, Glycobiology Research Unit, GlaxoWellcome Res. and Devt. Ltd., Medicines Research Centre, Stevenage, Herts, SG1 2NY, United Kingdom  
SOURCE: Glycobiology, (1998) 8/4 (321-327).

Refs: 35  
ISSN: 0959-6658 CODEN: GLYCE3  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The .alpha.3 fucosyltransferase, **FucT-VII**, is one of the key glycosyltransferases involved in the biosynthesis of the sialyl Lewis X (sLe(x)) antigen on human leukocytes. The sialyl Lewis X antigen (NeuAc.alpha.(2-3)Gal.beta.(1-4)[Fuc.alpha.(1-3)]GlcNAc-R) is an essential component of the recruitment of leukocytes to sites of inflammation, mediating the primary interaction between circulating leukocytes and activated endothelium. In order to characterize the enzymatic properties of the leukocyte .alpha.3 fucosyltransferase **FucT-VII**, the enzyme has been expressed in *Trichoplusia ni* insect cells. The enzyme is capable of synthesizing both sLe(x) and sialyl- dimeric-Le(x) structures in *vitro*, from 3'-sialyl-lacNAc and VIM-2 structures, respectively, with only low levels of fucose transfer observed to neutral or 3'-sulfated **acceptors**. Studies using fucosylated NeuAc.alpha.(2-3)- (Gal.beta.(1-4)GlcNAc)3-Me **acceptors** demonstrate that **FucT-VII** is able to synthesize both di-fucosylated and trifucosylated structures from mono-fucosylated precursors, but preferentially fucosylates the distal GlcNAc within a polylactosamine chain. Furthermore, the rate of **fucosylation** of the internal GlcNAc residues is reduced once fucose has been added to the distal GlcNAc. These results indicate that **FucT-VII** is capable of generating complex selectin ligands, in *vitro*, however the order of fucose addition to the lactosamine chain affects the rate of selectin ligand synthesis.

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

DUPLICATE 7

ACCESSION NUMBER: 1993:489859 CAPLUS

DOCUMENT NUMBER: 119:89859

TITLE: The cloning and expression of a human .alpha.-1,3  
**fucosyltransferase** capable of forming the  
E-selectin ligand

AUTHOR(S): Koszdin, Kari L.; Bowen, Benjamin R.

CORPORATE SOURCE: CIBA-GEIGY Corp., Summit, NJ, 07901, USA

SOURCE: Biochemical and Biophysical Research Communications  
(1992), 187(1), 152-7

CODEN: BBRCA9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The polymerase chain reaction was used to amplify a novel

**fucosyltransferase cDNA (FucT-VI)**

from A431 and from HL60 cells. The amplified **cDNA** has a high  
degree of sequence identity to FucT-V and to FucT-III, and a much lower  
level of similarity to FucT-IV. Transfection of the **FucT-**  
**VI** gene into mammalian cells confers .alpha.-1,3

**fucosyltransferase** activity to the cells, resulting in cell  
surface expression of Lewis x and sialyl-Lewis x carbohydrates. In  
contrast to FucT-IV activity, **FucT-VI** catalyzes the  
transfer of fucose from GDP-.beta.-fucose to .alpha.-2,3 sialylated  
substrates. The substrate specificity of the **FucT-VI**

gene product suggests that **FucT-VI** may be an enzyme  
involved in the biosynthesis of the E-selectin ligand, sialyl-Lewis x, in  
myeloid cells.

7, 8, 10, 13, 14, 16-19, 31, 40, 42,  
1, 8, 10, 13, 14, 16-19, 31-53  
2-8, 9, 12, 15, 20-21  
45-48, 49,  
50, 51

ACCESSION NUMBER: 1997:706974 CAPLUS

DOCUMENT NUMBER: 128:31742

TITLE: Acceptor specificity of GDP-  
Fuc:Gal.beta.1.fwdarw.4GlcNAc-R .alpha.3-**fucosyltransferase VI (FucT****VI)** expressed in insect cells as soluble,  
secreted enzymeAUTHOR(S): De Vries, Theodora; Palcic, Monica P.; Schoenmakers,  
Pascale S.; Van Den Eijnden, Dirk H.; Joziassse, David  
H.CORPORATE SOURCE: Department of Medical Chemistry, Vrije Universiteit  
Amsterdam, Amsterdam, NL-1081 BT, Neth.

SOURCE: Glycobiology (1997), 7(7), 921-927

CODEN: GLYCE3; ISSN: 0959-6658

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As an extension of a previous study (de Vries et al., 1995, J. Biol. Chem., 270, 8712-8722) the acceptor specificity of recombinant **FucT VI**, expressed in insect cells as sol. enzyme, and **purified** from the growth medium by affinity chromatog., was analyzed toward a broad panel of oligosaccharide and glycoprotein substrates. It was found that **FucT VI** effectively utilizes any type-2-chain based structure (Gal.beta.1.fwdarw.4GlcNAc-R). Neutral as well as sialylated structures are fucosylated with high efficiency. To identify polar groups on acceptors that function in enzyme

binding, deoxygenated substrate analogs were tested as acceptors. **FucT VI** had an abs. requirement for a hydroxyl at C-6 of galactose in addn. to the accepting hydroxyl at C-3. Thus, **FucT VI**, although different from FucT III, IV, and V in acceptor properties, seems to bind the acceptor in a similar way.



L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

DUPLICATE 4

ACCESSION NUMBER: 1998:645579 CAPLUS

DOCUMENT NUMBER: 130:1739

TITLE: Human .alpha.1,3/4-**fucosyltransferases** III.  
A Lys/Arg residue located within the .alpha.1,3-FucT motif is required for activity but not substrate binding

AUTHOR(S): Sherwood, Anne L.; Nguyen, Anton T.; Whitaker, Jeffery  
M.; Macher, Bruce A.; Stroud, Mark R.; Holmes, Eric H.

CORPORATE SOURCE: Division of Cell Surface Biochemistry, Northwest Hospital, Pacific Northwest Cancer Foundation, Seattle, WA, 98125, USA

SOURCE: Journal of Biological Chemistry (1998), 273(39), 25256-25260

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amino acid sequence alignment of human .alpha.1,3/4-**fucosyltransferases** (FucTs) demonstrates that three highly conserved Lys residues are present in the catalytic domain of FucTs III, IV, V, and VI. Two of these sites are conserved in **FucT VII**, with the third located within the .alpha.1,3-FucT motif as a conservative change to Arg at position 223. Site-directed mutagenesis expts. were conducted to change Lys255 of FucT V (equiv. to Arg223 of **FucT VII**) to either Arg255 or Ala255. Enzyme assays demonstrate that the FucT V K255R mutant has a 34-fold lower specific activity than native FucT V and that the K255A mutant is inactive. Site-directed mutagenesis of **FucT VII** was also conducted to change Arg223 to Lys223 for anal. of the effect on enzyme kinetic parameters. No differences in acceptor specificities or Km values

for either substrate were obsd. between native **FucT VII** and the R223K mutant; however, the **purified** R223K mutant enzyme had a 2-fold increased specific activity compared with **purified** native **FucT VII**. No change in GDP-fucose-protectable pyridoxal-P/NaBH4 inactivation was obsd. for native or mutant FucT V or VII, further supporting the absence of involvement of this residue in sugar nucleotide binding. The results indicate that a basic residue in this position is required for enzyme activity, with a Lys residue providing higher intrinsic activity. The lack of influence of this site on substrate binding parameters and its location within the .alpha.1,3-FucT motif suggest that at least some of the residues within this motif are involved in catalysis rather than substrate binding.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE